POOLED SAFETY OF ELINZANETANT FOR THE TREATMENT OF VASOMOTOR SYMPTOMS ASSOCIATED WITH MENOPAUSE ACROSS THE US POPULATION FROM 4 PLACEBO-CONTROLLED STUDIES

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INTRODUCTION

- Elinzanetant is a dual neurokinin (NK)-targeted therapy (NK1 and NK3 receptor antagonist) for the treatment of moderate-to-severe vasomotor symptoms (M/S VMS), also known as hot flashes, in postmenopausal women
- Elinzanetant was investigated in the Phase IIb SWITCH-1 study, which determined the optimal dose of elinzanetant to be 120 mg[1]
- The 2 Phase III studies, OASIS-1 and OASIS-2, demonstrated the efficacy of elinzanetant in reducing the frequency and severity of VMS and additionally in improving sleep disturbances and quality of life vs placebo in women with ≥50 VMS per week[2]
- The OASIS-3 study further supported the sustained efficacy and safety of elinzanetant over 52 weeks (there was no VMS threshold at baseline in the OASIS-3 study)[3]

- This post hoc analysis evaluated the overall safety and tolerability of elinzanetant in US and non-US women with M/S VMS associated with menopause, using pooled data from SWITCH-1, OASIS-1, OASIS-2, and OASIS-3

METHODS

Study design and participants

- US subgroup analysis from 4 double-blind, randomized, placebo-controlled, multinational trials
- Naturally or surgically postmenopausal US women aged 40–65 years experiencing M/S VMS who received elinzanetant 120 mg or placebo

SWITCH-1[1]

Phase IIb study randomized women 1:1:1:1:1 to receive elinzanetant 40, 80, 120, or 160 mg or placebo for 12 weeks

OASIS-1 and OASIS-2[2]

Phase III studies randomized women 1:1 to receive either elinzanetant 120 mg for 26 weeks, or placebo for 12 weeks followed by elinzanetant for 14 weeks

OASIS-3[3]

Phase III study randomized women 1:1 to receive 120 mg elinzanetant or placebo for 52 weeks

Endpoints

- Treatment-emergent adverse events (TEAEs) across all 4 studies over 52 weeks
- Exposure-adjusted incidence rates (EAIRs; per 100 patient-years) for elinzanetant vs placebo
- Most frequently reported TEAEs
- TEAE severity (mild, moderate, or severe)
- Treatment discontinuations due to TEAEs

RESULTS

Baseline demographics

- A total of 690 US women were included in the study (**Table 1**); 343 participants received elinzanetant 120 mg and 347 received placebo for the first 12 weeks. Across weeks 1–52, 516 participants received elinzanetant and 347 received placebo

	US safety population (N=690)	Non-US population (N=829)
White, n (%)	425 (61.6)	783 (94.5)
Black or African American, n (%)	238 (34.5)	9 (1.1)
Asian, n (%)	7 (1.0)	3 (0.4)
American Indian or Alaska Native, n (%)	4 (0.6)	0
Other, n (%)[a]	16 (2.3)	34 (4.1)
Age, years, mean (SD)	55.2 (4.9)	54.3 (4.7)
Smoking, never, n (%)	404 (58.6)	476 (57.4)
BMI, kg/m², mean (SD)	28.9 (5.0)	26.7 (4.2)

Table 1. Baseline characteristics of the US vs the non-US safety population. BMI, body mass index; SD, standard deviation. [a]Native Hawaiian or Other Pacific Islander, multiple, other, or not reported.

Overview of TEAEs during weeks 1–52

- TEAEs were experienced by 259 (50.2%) elinzanetant-treated and 163 (47.0%) placebo-treated patients (**Table 2**)
- EAIRs were 169.67 per 100 patient-years in elinzanetant-treated patients and 187.61 per 100 patient-years in placebo-treated patients
- Of the patients experiencing a TEAE, most were of mild or moderate maximum intensity

	Elinzanetant 120 mg (n=516)[a]		Placebo (n=347)[a]	
	n (%)	EAIR/100 py	n (%)	EAIR/100 py
Any AE	259 (50.2)	169.67	163 (47.0)	187.61
Maximum intensity for any AE				
Mild	147 (28.5)		84 (24.2)	
Moderate	94 (18.2)		67 (19.3)	
Severe	18 (3.5)		12 (3.5)	
Any study drug–related AE	75 (14.5)	31.69	37 (10.7)	31.35
Maximum intensity for study drug–related AE				
Mild	46 (8.9)		23 (6.6)	
Moderate	27 (5.2)		12 (3.5)	
Severe	2 (0.4)		2 (0.6)	
Any SAE	15 (2.9)	6.28	7 (2.0)	4.66
Any study drug–related SAE	1 (0.2)	0.33	0	

Table 2. Overview of TEAEs during weeks 1–52. 100 py, 100 patient-years; AE, adverse event; EAIR, exposure-adjusted incidence rate; SAE, serious adverse event; TEAE, treatment-emergent adverse event. [a]The total US population exceeded 690 because the elinzanetant group included those who switched from placebo to elinzanetant after 12 weeks in OASIS-1 and OASIS-2.

Most frequently reported TEAEs and TEAEs of special interest during weeks 1–52

- The most frequently reported TEAEs were headache and coronavirus disease 2019 (COVID-19) (**Table 3**)
- There were no reported cases of endometrial hyperplasia or malignant neoplasms (**Table 4**)
- Increased alanine aminotransferase and aspartate aminotransferase were reported in 2 (0.4%) and 3 (0.6%) participants treated with elinzanetant, respectively (all were mild) (**Table 4**)

	Elinzanetant 120 mg (n=516)[a]		Placebo (n=347)[a]	
	n (%)	EAIR/100 py	n (%)	EAIR/100 py
Headache	25 (4.8)	9.95	10 (2.9)	8.38
COVID-19	22 (4.3)	10.01	19 (5.5)	12.70
Urinary tract infection	21 (4.1)	7.96	8 (2.3)	5.11
Fatigue	14 (2.7)	5.29	5 (1.4)	4.09
Arthralgia	13 (2.5)	4.74	10 (2.9)	9.33
Upper respiratory tract infection	11 (2.1)	4.51	14 (4.0)	9.72
Gastroesophageal reflux disease	11 (2.1)	4.07	5 (1.4)	2.93
Depression	10 (1.9)	3.74	8 (2.3)	6.67
Increased depression rating score	11 (2.1)	3.64	8 (2.3)	8.38
Somnolence	7 (1.4)	2.76	1 (0.3)	0.46

Table 3. Most frequently reported TEAEs during weeks 1–52. 100 py, 100 patient-years; COVID-19, coronavirus disease 2019; EAIR, exposure-adjusted incidence rate; TEAE, treatment-emergent adverse event. [a]The total US population exceeded 690 because the elinzanetant group included those who switched from placebo to elinzanetant after 12 weeks in OASIS-1 and OASIS-2.

	Elinzanetant 120 mg (n=516)[a]		Placebo (n=347)[a]	
	n (%)	EAIR/100 py	n (%)	EAIR/100 py
Alanine aminotransferase increased	2 (0.4)	0.87	1 (0.3)	0.46
Mild	2 (0.4)		1 (0.3)	
Aspartate aminotransferase increased	3 (0.6)	1.07	1 (0.3)	0.47
Mild	3 (0.6)		0	
Moderate	0		1 (0.3)	
Alkaline phosphatase increased	1 (0.2)	0.33	0	
Mild	1 (0.2)		0	
Bilirubin increased	1 (0.2)	0.33	0	
Mild	1 (0.2)		0	
Endometrial hyperplasia	0		0	
Malignant endometrial neoplasms	0		0	

Table 4. TEAEs of special interest during weeks 1–52. 100 py, 100 patient-years; EAIR, exposure-adjusted incidence rate; TEAE, treatment-emergent adverse event. [a]The total US population exceeded 690 because the elinzanetant group included those who switched from placebo to elinzanetant after 12 weeks in OASIS-1 and OASIS-2.

- Overall, 51 women discontinued treatment due to TEAEs[a]
- 37 (7.2%) women in the elinzanetant group vs 14 (4%) women in the placebo group discontinued treatment due to TEAEs
- The most commonly reported TEAEs leading to treatment discontinuation in the elinzanetant group were fatigue (n=7 [1.4%]), headache (n=4 [0.8%]), arthralgia (n=3 [0.6%]), and nausea (n=3 [0.6%])

[a]Number of patients with ≥1 event.

KEY TAKEAWAYS

This pooled safety analysis of data from 690 US women from 4 studies supports the safety of elinzanetant 120 mg for the treatment of M/S VMS during menopause

Elinzanetant was well tolerated for up to 52 weeks of treatment

- Most TEAEs were mild or moderate in intensity
- Headache and COVID-19 were the most frequently reported TEAEs
- Fatigue was the most common TEAE leading to treatment discontinuation with elinzanetant 120 mg
- No hepatotoxicity or endometrial safety concerns were noted

The safety of elinzanetant within the US population was similar to the safety observed in the full multinational population

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ACKNOWLEDGMENTS

This study was sponsored by Bayer U.S. (Whippany, NJ, USA). Medical writing assistance was provided by Katy Beck, PhD, and Sara Edwards, MSc, of Envision Catalyst, an Envision Medical Communications agency, a part of Envision Pharma Group.

DISCLOSURES

James A. Simon: received grant/research support from AbbVie, Bayer, Madorra, Mylan/Viatris, Myovant, Sola Pelvic Therapy, and Viking; consultant/advisory boards for Ascend, Bayer, Besins, Biote, Cosette, Femasys, Mayne, Pfizer, and Vella; speaker's bureaus/fees for Ascend, Besins, Lawley, Mayne, Myovant, and Pharmavite; stockholder (direct purchase) in Sermonix. Barbara Yaeger: employee of Bayer U.S. (Boulder, CO, USA). Andrew M. Kaunitz: employer (University of Florida) has received research funding from Bayer. Maja Francuski: employee of Bayer AG (Berlin, Germany). Andrew Trigg: employee of Bayer plc (Reading, UK). Gloria Bachmann: nothing to disclose.

Presented at the American College of Obstetricians and Gynecologists (ACOG) 2026 Annual Clinical & Scientific Meeting; May 1–3, 2026; Washington, DC, USA. Previously presented at The Menopause Society Annual Meeting; October 21–25, 2025; Orlando, FL, USA